VERSION WITH MARKINGS TO SHOW CHANGES MADE

IN THE SPECIFICATION:

Paragraph beginning at page 9, line 8, has been amended as follows:

[Sequences No. 1 and No. 2] SEQ ID NO: 1 and SEQ ID NO: 2 in the Sequence Table are the DNA sequence of the ribosomal protein L7/L12 gene of *Haemophilus influenzae* and corresponding amino acid sequence. [Sequences No. 3 and No. 4] SEQ ID NO: 3 and SEQ ID NO: 4 are the DNA sequence of the ribosomal protein L7/L12 gene of *Helicobacter pylori* and the corresponding amino acid sequence. [Sequences No. 5 and No. 6] SEQ ID NO: 5 and SEQ ID NO: 6 show the DNA sequence and the corresponding amino acid sequence of the ribosomal protein L7/L12 gene of *Streptococcus pneumoniae*. [Sequences No. 7 and No. 8] SEQ ID NO: 7 and SEQ ID NO: 8 show the DNA sequence and the corresponding amino acid sequence of the ribosomal protein L7/L12 gene of *Neisseria gonorrhoeae*. [Sequences No. 9 and No. 10] SEQ ID NO: 9 and SEQ ID NO: 10 show the DNA sequence and the corresponding amino acid sequence of the ribosomal protein L7/L12 gene of *Neisseria meningitidis*. [Sequence No. 11 and Sequence No. 12] SEQ ID NO: 11 and SEQ ID NO: 12 in the Sequence Table are the primers DNA for PCR used to acquire the ribosomal protein L7/L12 gene from *Haemophilus influenzae*. [Sequences No. 13 and No. 14] SEQ ID NO: 13 and SEQ ID NO: 14 in the Sequence Table are the primer DNA for PCR used to acquire the ribosomal protein L7/L12 gene from

Streptococcus pneumoniae. [Sequences No. 15 and No. 16] SEQ ID NO: 15 and SEQ ID NO: 16 in the Sequence Table are the primer DNA for PCR used to acquire the ribosomal protein L7/L12 gene from *Neisseria gonorrhoeae*. [Sequences No. 17 and No. 18] SEQ ID NO: 17 and SEQ ID NO: 18 show the DNA sequence and the corresponding amino acid sequence of the ribosomal protein L7/L12 gene of *Haemophilus influenzae*. [Sequences No. 19 and No. 20] SEQ ID NO: 19 and SEQ ID NO: 20 show the DNA sequence and the corresponding amino acid sequence of the ribosomal protein L7/L12 gene of *Streptococcus pneumoniae*. [Sequences No. 21 and No. 22] SEQ ID NO: 21 and SEQ ID NO: 22 show the DNA sequence and the corresponding amino acid sequence of the ribosomal protein L7/L12 gene of *Neisseria gonorrhoeae*.

Paragraph beginning at page 19, line 3, has been amended as follows:

The amino acid and DNA sequence of ribosomal protein L7/L12 of *Haemophilus influenzae* are shown in ["Sequences No. 1 and No. 2."] SEQ ID NO: 1 and SEQ ID NO: 2.

Paragraph beginning at page 19, line 6, has been amended as follows:

Consequently, in the case of this bacteria, it is possible to similarly compare the amino acid sequence of ribosomal protein L7/L12 with the same protein of, for instance, *Helicobacter pylori*, which is shown in ["Sequence No. 3 and No. 4,"] SEQ ID NO: 3 and SEQ ID NO: 4, and synthesize a peptide of 5

to 30 amino acids for the segment of low homology and make polyclonal antibody or monoclonal antibody specific to *Haemophilus influenzae* using this peptide.

Paragraph beginning at page 19, line 21, has been amended as follows:

Moreover, PCR primers based on the sequences of N-terminal and C-terminal, for example, the PCR primers shown in [Sequences No. 11 and No. 12] SEQ ID NO: 11 and SEQ ID NO: 12 in the Sequence Table, were designed from the DNA sequence of ribosomal protein L7/L12 of *Haemophilus influenzae*. Utilizing homology of the PCR primers, DNA fragments amplified by the PCR method or the like using genomic DNA which is extracted from cultivated *Haemophilus influenzae* can be acquired by a conventional method. The entire length of the gene for ribosomal protein L7/L12 of *Haemophilus influenzae* can be acquired by the analysis of the DNA sequence information of these fragments.

Paragraph beginning at page 20, line 26, has been amended as follows:

Moreover, the amino acid sequence and the DNA sequence of ribosomal protein L7/L12 of *Streptococcus pneumoniae* which is also highly significant as a diagnostic agent for respiratory infection diseases as well as *Haemophilus influenzae*, are known from descriptions in data bases and the like. The amino acid and DNA sequences of ribosomal protein L7/L12 of *Streptococcus*

pneumoniae are shown in [Sequences No. 5 and No. 6] SEQ ID NO: 5 and SEQ ID NO: 6 of sequence table.

Paragraph beginning at page 21, line 8, has been amended as follows:

It is therefore possible to acquire a polyclonal antibody or monoclonal antibody which is specific to *Streptococcus pneumoniae* by designing a PCR primer, the PCR primer shown by [Sequence ID No. 13 or 14] SEQ ID NO: 13 or SEQ ID NO: 14 in the Sequence Table, for example, based on the sequences of N-terminal and C-terminal of DNA sequence of Ribosomal Proteins L7/L12 of *Streptococcus pneumoniae* in the same manner as in the case of *Haemophilus influenzae*, and processing thereafter in the same manner as in the case of *Haemophilus influenzae*.

Paragraph beginning at page 22, line 10, has been amended as follows:

When part of the known DNA sequence of ribosomal protein L7/L12 was used to probe the existence of DNA fragments with a similar sequence, it was found that DNA sequence corresponding to the ribosomal protein L7/L12 gene is present and it was possible to obtain data on its entire DNA sequence. The entire base sequence and corresponding amino acid sequence fo the ribosomal protein L7/L12 gene of this *Neisseria gonorrhoeae* are shown in [Sequences No. 7 and No. 8] SEQ ID NO: 7 and SEQ ID NO: 8 of the sequence table.

Paragraph beginning at page 22, line 20, has been amended as follows:

It is therefore possible to acquire the target antibody which is specific to *Neisseria gonorrhoeae* having the entire or partial Ribosomal Protein L7/L12 of *Neisseria gonorrhoeae* as an antigen by designing a PCR primer, the PCR primer shown by [Sequence ID No. 15 or 16] SEQ ID NO: 15 or SEQ ID NO: 16 in the Sequence Table, for example, based on the sequences of N-terminal and C-terminal of DNA sequence of Ribosomal Protein L7/L12 of *Neisseria gonorrhoeae* in the same manner as in the case of *Haemophilus influenzae*, and *Strepcoccus pneumoniae*, and processing thereafter in exactly the same manner as in the case of *Haemophilus influenzae* or *Streptococcus pneumoniae*.

Paragraph beginning at page 23, line 6, has been amended as follows:

Particularly, the gene sequence of ribosomal protein L7/L12 fo *Neisseria meningitides*, which belongs to the same *Neisseria* genus as *Neisseria gonorrhoeae* is disclosed and readily available on the Internet. The entire base sequence and the corresponding amino acid sequence of the ribosomal protein L7/L12 gene of *Neisseria meningitides* are shown in ["Sequences No. 9 and No. 10."] SEQ ID NO: 9 and SEQ ID NO: 10. Here, comparing the entire base sequence for ribosomal protein L7/L12 genes of *Neisseria meningitidis* and *Neisseria gonorrhoeae*, only difference in the amino acid sequence is that Neisseria gonorrhoeae has

alanine for the 115th amino acid from the N-terminal, whereas *Neisseria meningitidis* has glutamic acid. Therefore, it can be concluded that the antibody for the ribosomal protein L7/L12 of *Neisseria gonorrhoeae* which can specifically detects *Neisseria gonorrhoeae* is the antibody which identifies alanine at 115 from the N-terminal and the amino acid region including the alanine of ribosomal protein L7/L12 as an epitope.

Paragraph beginning at page 24, line 25, has been amended as follows:

After inoculating an appropriate amount of *Haemophilus influenzae* strain ATCC93334 (IID984) (obtained from Tokyo University School of Medicine Laboratories) in a chocolate agar culture medium, the strain was cultivated for 24 hours in a CO_2 incubator under conditions of 37 °C and [0.5 <5.0> %] 5.0% CO_2. The colonies that grew were suspended in a TE buffer (manufactured by Wako Pure Chemical Co., Ltd.) to a final concentration of approximately 5 x 10^9 CFU/ml. Approximately 1.5 ml of this suspension was transferred to a microcentrifuge tube and centrifuged for 2 minutes at 10,000 rpm. The supernatant was discarded. The sediment was resuspended in 567 µl TE buffer. Then 30 µl 10 % sodium dodecylsulfate (SDS) and 3 µl 20 mg/ml Proteinase K solution were added and thoroughly mixed. The suspension was incubated for another hour at 37°C. Next, after adding 80 µl 10 % cetyl trimethyl ammonium bromide/0.7 M NaCl solution and thoroughly mixing the product, it was incubated for

10 minutes at 65 °C. Next, 700 µl chloroform-isoamyl alcohol solution at a volume ratio of 24:1 was added and stirred well. The solution was centrifuged for 5 minutes (while being kept at 4 °C) at 12,000 rpm using a microcentrifugation device and the aqueous fraction was transferred to a new microtube. Isopropanol was added to the fraction at 0.6-times its volume and the tube was vigorously shaken to form sediment of the DNA. The white DNA sediment was scooped with a glass rod and transferred to a different microcentrifuge tube containing 1 ml 70% ethanol (cooled to -20 °C).

Paragraph beginning at page 28, line 11, has been amended as follows:

Determination of the base sequence of the inserted DNA fragment was performed using the Fluorescence Sequencer of Applied Biosystems. The sequence sample was prepared using PRISM, Ready Reaction Dye Terminator Cycle Sequencing Kit (Applied Biosystems). First, 9.5 µl reaction stock solution, 4.0 µl T7 promoter primer at 0.8 pmol/µl (Gibco BRL) and 6.5 µl of template DNA for sequencing at 0.16 µg/µl were added to a microtube with a capacity of 0.5 ml, mixed and superposed with 100 µl mineral oil. PCR amplification was performed for 25 cycles, where one cycle consisted of 30 seconds at 96 °C, 15 seconds at 55 °C, and 4 minutes at 60 °C. The product was then kept at 4 °C for 5 minutes. After the reaction was completed, 80 µl sterilized pure water was added and stirred. The product was

centrifuged and the aqueous layer was extracted 3 times with phenol-chloroform. [Ten ml] 10 µl <microliters> 3 M sodium acetate (pH 5.2) and 300 µl ethanol were added to 100 µl aqueous layer and stirred. The product was then centrifuged for 15 minutes at room temperature and 14,000 rpm and the sediment was recovered. Once the sediment was washed with 75 % ethanol, it was dried under a vacuum for 2 minutes to obtain the sequencing sample. The sequencing sample was dissolved in formamide containing 4 µl 10 mM EDTA and denatured for 2 minutes at 90 °C. This was then cooled in ice and applied to sequencing.

Paragraph beginning at page 29, line 12, has been amended as follows:

One of the 5 clones obtained had homology of the sequence with the probe used for PCR. In addition, DNA sequences extremely similar to the gene sequence of ribosomal protein L7/L12 gene of the other microorganisms, for example, *Neisseria gonorrhoeae*, were discovered. The entire base sequence and the corresponding amino acid sequence of the structural gene moiety are as shown in [Sequence ID No. 17 and No. 18] SEQ ID NO: 17 and SEQ ID NO: 18 of the Sequence Table. This gene fragment clearly codes for *Haemophilus influenzae* ribosomal protein L7/L12.

Paragraph beginning at page 40, line 14, has been amended as follows:

PCR was performed using 10 ng of this genomic DNA. Taq polymerase (Takara Co., ltd., code R001A) was employed for PCR.

Then 5 µl of buffer attached to enzyme, 4 µl dNTP mixture attached to enzyme, and 200 pmol each of synthetic oligonucleotide C shown in [Sequence No. 13] SEQ ID NO: 13 of the Sequence Table and synthetic oligonucleotide D shown in [Sequence No. 14] SEQ ID NO: 14 of the Sequence table were added to the enzyme to bring the final volume to 50 µl.

Paragraph beginning at page 54, line 7, has been amended as follows:

After inoculating an appropriate amount of *Neisseria gonorrhoeae* strain IID821 (obtained from Tokyo University School of Medicine Laboratories) in a chocolate agar culture medium, the strain was cultivated for 24 hours in a CO_2 incubator under conditions of 37 °C and [0.5 <5.0> %] 5.0% CO_2. The colonies that grew were suspended in a TE buffer to a final concentration of approximately 5 x 10^9 CFU/ml. Approximately 1.5 ml of this suspension was transferred to a microcentrifugation tube and centrifuged for 2 minutes at 10,000 rpm. The supernatant was discarded. The sediment was resuspended in 567 µl TE buffer. Then 30 µl 10 % SDS and 3 µl 20 mg/ml Proteinase K solution were added and thoroughly mixed. The suspension was incubated for another hour at 37 °C.

Paragraph beginning at page 55, line 24, has been amended as follows:

PCR was performed using 10 ng of this genomic DNA. PCR was performed using Taq polymerase (Takara Co., Ltd., code

R001A). Then, 5 µl of a buffer attached to enzyme, 4 µl of a dNTP mixture attached to enzyme, and 200 pmol each of synthetic oligonucleotide E shown in [Sequence No. 15] SEQ ID NO: 15 of the Sequence Table and synthetic oligonucleotide F shown in [Sequence No. 16] SEQ ID NO: 16 of the Sequence Table, which were designed based on the ribosomal protein L7/L12 DNA sequence of *Neisseria gonorrhoeae* acquired from Internet Information (Oklahoma University, *N. Gonorrhoeae* Genome Project, disclosed genomic DNA data) because of the similarity with ribosomal protein L7/L12 DNA sequence of other bacteria, were added to the enzyme to bring the final volume to 50 µl.

Paragraph beginning at page 57, line 23, has been amended as follows:

Determination of the base sequence of the inserted DNA fragment was performed using the Fluorescence Sequencer of Applied Biosystems. The sequence sample was prepared using PRISM, Ready Reaction Dye Terminator Cycle Sequencing Kit (Applied Biosystems). First, 9.5 µl reaction stock solution, 4.0 µl T7 promoter primer at 0.8 pmol/µl (Gibco BRL) and 6.5 µl template DNA for sequencing at 0.16 µg/µl were added to a microtube with a capacity of 0.5 ml and mixed. After layering with 100 µl mineral oil, PCR amplification was performed for 25 cycles, where one cycle consisted of 30 seconds at 96 °C, 15 seconds at 55 °C, and 4 minutes at 60 °C. The product was then kept at 4 °C for 5 minutes. After the reaction was completed, 80

µl sterilized pure water was added and stirred. The product was centrifuged and the aqueous layer was extracted 3 times with phenol-chloroform. Ten microliters 3 M sodium acetate (pH 5.2) and 300 µl ethanol were added to 100 µl aqueous layer and stirred. The product was then centrifuged for 15 minutes at room temperature and 14000 rpm and the sediment was recovered. Once the sediment was washed with 75 % ethanol, it was dried under a vacuum for 2 minutes to obtain the sequencing sample. The sequencing sample was dissolved in formamide containing 4 µl 10 mM EDTA and denatured for 2 minutes at 90 °C. This was then cooled in ice and submitted to sequencing. One of the 5 clones obtained had homology of the sequence with the probe used for PCR. In addition, DNA sequences extremely similar to the gene sequence of ribosomal protein L7/L12 gene of the other microorganisms, for example, *Haemophilus influenzae*, were discovered. The entire base sequence and the corresponding amino acid sequence of the structural gene moiety are as shown in [Sequence No. 21 and No. 22] SEQ ID NO: 21 and SEQ ID NO: 22 of the Sequence Table. This gene fragment clearly codes for ribosomal protein L7/L12 gene of *Neisseria gonorrhoeae*.

Paragraph beginning at page 63, line 5, has been amended as follows:

After inoculating an appropriate amount of *Neisseria gonorrhoeae* strain IID821 (obtained from Tokyo University School of Medicine Laboratories) in a chocolate agar culture medium, the

strain was cultivated for 24 hours in a CO_2 incubator under conditions of 37 °C and [0.5 <5.0> %] 5.0% CO_2. The colonies that grew were suspended in a TE buffer to a final concentration of approximately 5 x 10^9 CFU/ml. Approximately 1.5 ml of this suspension was transferred to a microcentrifugation tube and centrifuged for 2 minutes at 10,000 rpm. The supernatant was discarded. The sediment was resuspended in 567 µl TE buffer. Then 30 µl 10 % SDS and 3 µl 20 mg/ml Proteinase K solution were added and thoroughly mixed. The suspension was incubated for another hour at 37 °C. Next, after adding 80 µl 10 % cetyl trimethyl ammonium bromide/0.7 M NaCl solution and thoroughly mixing the product, it was incubated for 10 minutes at 65 °C. Next, 700 µl chloroform-isoamyl alcohol solution at a volume ratio of 24:1 was added and stirred well.

Paragraph beginning at page 84, line 10, has been amended as follows:

After inoculating an appropriate amount of *Neisseria gonorrhoeae* strain IID821 (obtained from Tokyo University School of Medicine Laboratories) in a chocolate agar culture medium, the strain was cultivated for 24 hours in a CO_2 incubator under conditions of 37 °C and [0.5 <5.0> %] 5.0% CO_2. The colonies that grew were suspended in a TE buffer to a final concentration of approximately 5 x 10^9 CFU/ml. Approximately 1.5 ml of this suspension was transferred to a microcentrifugation tube and centrifuged for 2 minutes at 10,000 rpm. The supernatant was

discarded. The sediment was resuspended in 567 µl TE buffer. Then 30 µl 10 % SDS and 3 µl 20 mg/ml Proteinase K solution were added and thoroughly mixed. The suspension was incubated for another hour at 37 °C. Next, after adding 80 µl 10 % cetyl trimethyl ammonium bromide/0.7 M NaCl solution and thoroughly mixing the product, it was incubated for 10 minutes at 65 °C. Next, 700 µl chloroform-isoamyl alcohol solution at a volume ratio of 24:1 was added and stirred well. The solution was centrifuged for 5 minutes (while being kept at 4 °C) at 12,000 rpm using a microcentrifugation device and the aqueous fraction was transferred to a new microtube. Isopropanol was added to the fraction at 0.6-times its volume and the tube was vigorously shaken to form sediment of the DNA. The white DNA sediment was scooped with a glass rod and transferred to a different microcentrifugation tube containing 1 ml 70 % ethanol (cooled to -20 °C).

Paragraph beginning at page 85, line 26, has been amended as follows:

PCR was performed using 10 ng of this genomic DNA. Taq polymerase (Takara Co., Ltd., code R001A) was employed for PCR. Then, 5 µl of a buffer attached to enzyme, 4 µl of dNTP mixture attached to enzyme, and 200 pmol of each of synthetic oligonucleotide E shown in [Sequence No. 15] SEQ ID NO: 15 of the Sequence Table and synthetic oligonucleotde F shown in [Sequence No. 16] SEQ ID NO: 16 of the Sequence Table, which were designed

based on the ribosomal protein L7/L12 DNA sequence of *Neisseria gonorrhoeae* acquired from Internet information (Oklahoma University, *N. Gonorrhoeae* Genome Project, disclosed genomic DNA data) because of the familiarity with ribosomal protein L7/L12 DNA sequence of other bacteria, were added to the enzyme to bring the final volume to 50 µl.

Paragraph beginning at page 87, line 26, has been amended as follows:

Determination of the base sequence of the inserted DNA fragment was performed using the Fluorescence Sequencer of Applied Biosystems. The sequence sample was prepared using PRISM, Ready Reaction Dye Terminator Cycle Sequencing Kit (Applied Biosystems). First, 9.5 µl reaction stock solution, 4.0 µl T7 promoter primer at 0.8 pmol/µl (Gibco BRL) and 6.5 µl template DNA for sequencing at 0.16 µg/µl were added to a microtube with a capacity of 0.5 ml and mixed. After superposition with 100 µl mineral oil, PCR amplification was performed for 25 cycles, where one cycle consisted of 30 seconds at 96 °C, 15 seconds at 55 °C, and 4 minutes at 60 °C. The product was then kept at 4 °C for 4 minutes. After the reaction was completed, 80 µl sterilized pure water was added and stirred. The product was centrifuged and the aqueous layer was extracted 3 times with phenol-chloroform. Ten microliters 3 M sodium acetate (pH 5.2) and 300 µl ethanol were added to 100 µl aqueous layer and stirred. The product was then centrifuged for 15 minutes at

room temperature and 14,000 rpm and the sediment was recovered. Once the sediment was washed with 75 % ethanol, it was dried under a vacuum for 2 minutes to obtain the sequencing sample. The sequencing sample was dissolved in formamide containing 4 µl 10 mM EDTA and denatured for 2 minutes at 90 °C. This was then cooled in ice and submitted to sequencing. One of the 5 clones obtained had homology of the sequence with the probe used for PCR. In addition, DNA sequences extremely similar to the gene sequence of ribosomal protein L7/L12 gene of the other microorganisms, for example, *Haemophilus influenzae*, were discovered. The entire base sequence and the corresponding amino acid sequence of the structural gene moiety are as shown in [Sequence No. 21 and No. 22] SEQ ID NO: 21 and SEQ ID NO: 22 of the Sequence Table. This gene fragment clearly codes for *Neisseria gonorrhoeae* ribosomal protein L7/L12.

IN THE CLAIMS:

Claim 8 has been amended as follows:

8. (amended) The antibody according to claim 7, which is the antibody to ribosomal protein L7/L12 of *Neisseria gonorrhoeae* and which recognizes a continuous amino acid sequence moiety from 5 to 30 amino acids including the 115th alanine in the amino acid sequence of [Sequence ID No. 22] SEQ ID NO: 22 of the Sequence Table.